Closing the Loop on Critical Care Life Support for Military *En Route* Care Environments+

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SUMMARY

The Future Force (FF) war-fighting concept includes maintenance of medical functionality as close to the action as possible for 72 hrs without re-supply and possibly without air evacuation assets. The most challenging casualty for the Forward Surgical Team (FST) is the critically injured soldier requiring immediate life-saving surgery and transport while on life support equipment. The FF battlefield envisions long evacuation distances, exceeding the 2 hr., flight capabilities of the current UH60 Blackhawk used for MEDEVAC. This situation requires greater holding capability at the FST and enhanced en route care capabilities in both ground and air evacuation vehicles with 10 to 12 hour transport times. The Automated Critical Care Life Support (ACCLS) capability under development within the US Army's Medical Research and Materiel Command, will provide automation of life support functions, through the development of computer-driven closed loop control of ventilation, fluid, drug and oxygen administration. This closed loop approach to life support will not only optimize the patient's life support but will result in significant conservation of IV fluid and oxygen resuscitation resources.

1.0 INTRODUCTION

Clearing the battlefield quickly and efficiently while providing the patient the best possible care is a priority mission of the US tri-service, military medical community. At the same time, reduction in the size of the medical footprint and enhancement of the mobility of our MTFs is also a high priority. Expedient movement of the critical care patient population would contribute significantly to the attainment of these goals [20]. Since World War II, 90% of all combat battle deaths occurred within the first hour in Echelon I before reaching the first level of medical care. This statistic has remained unchanged thru the Viet Nam War. Hemorrhage and CNS trauma were the leading factors that contributed to early death of these casualties.

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Although a small fraction of the total casualty population, about 10% requiring immediate surgery these patients require a disproportionately large number of man-hours and logistical support in the field. [16]

Current US military evacuation procedures require that a patient be held in a field MTF until ready to return to duty or until stable enough to be evacuated [6]. For the critical patient, this can be several days or more before he can withstand the added stresses of ground or air evacuation with the attendant high ambient noise and vibration, and in the case of rotor-wing air evacuation and the MV22, low atmospheric pressure conditions. Although there is little reason to believe that the high acoustic noise and vibration are, in themselves, medical hazards, they would, and do, significantly degrade the attendant care-giver's diagnostic and therapeutic capabilities *en route*. Heart and lung sounds are difficult if not impossible to detect above road or aircraft noise and even simple palpation of peripheral pulses can be very challenging if not impossible in the hypotensive patient, in high vibration environments. In addition, the training of the air and ground medics attending these patients does not include management of the critically injured on life support equipment. These conditions create a significant hazard for the patient since a medical crisis may escape detection en route. On the other hand, delaying the evacuation for the time required to get the patient off his life support equipment is not desirable either as this compromises the mobility of the Forward Surgical Team which is charged to stay within a few miles of the forward edge of the battlefield. It is for these reasons that a portable, lightweight, self-contained system that provides capability for continuous monitoring of casualty status, including assessment of early markers of physiological deterioration, automated alarming, and closed-loop, automatic control of life support equipment and interventions would be of value to medical personnel after casualty stabilization and during evacuation.

1.1 Military Rationale for Closed Loop Life Support

The key to successful management of the critically ill patient is vigilance. Monitoring the patient with sufficient frequency to detect life-threatening events early enough to implement lifesaving therapy is challenging enough in the controlled civilian hospital environment. However, this challenge is magnified enormously when care of the critically ill patient on life support equipment is taken into the battlefield setting, where personnel and supply constraints are much greater and the vigilance factor is further compromised by environmental challenges such as high noise, and in the Medevac setting, high vibration. The goal of any critical care unit, through both staffing efforts and the design of effective alarm systems within the monitoring equipment, is to minimize the time between detection of life-threatening events and the implementation of a corrective or therapeutic action. Computerized monitoring combined with digital control capabilities built into life support equipment offers an opportunity to automatically accomplish this goal and offers the possibility of significantly enhancing the responsiveness of the life support system.

The Army Transformation's FF Force (FF) war-fighting concept, includes maintenance of medical functionality as close to the action as possible for 72 hrs without re-supply and possibly without air evacuation assets. The most challenging casualty for the Forward Surgical Team (FST) is the critically injured soldier requiring immediate life-saving surgery and life support equipment. The FF battlefield envisions long evacuation distances, exceeding the 2 hr., flight capabilities of the current UH60 Blackhawk used for MEDEVAC. This situation requires greater holding capability at the FST and enhanced en route care capabilities in both ground and air evacuation vehicles with 10 to 12 hour transport times. The ACCLS capability proposed here would provide automation of life support functions, providing computer-driven closed loop control of ventilation, fluid, drug and oxygen administration in the first iteration. This system would optimize the patient's treatment, while minimizing resource utilization (i.e. oxygen and resuscitation fluid). The ACCLS platform will also be a significant critical care enabler for the small FST staff and for the 91W staffing of air and ground ambulances. Currently, ambulance medical attendants are not trained critical

care specialists, a situation not anticipated to change in the FF. Therefore, automation of the life support systems is a critical capability that will allow expedient movement of casualties out of the FST and will level the quality of care throughout the echelons of medical care of the critically injured. The system will also provide data logging and telecommunication capability to facilitate record keeping and to enable real time communication of patient data to the receiving hospital for assistance with monitoring and decision assistance from a remote location. The ACCLS will provide increased and improved holding capability at the FST as well as extended critical care capability within the ground ambulance platform by providing automated life support for the critically injured awaiting and during evacuation.

1.2 Requirements for the ACCLS System

1.2.1 Hardware

The physical requirements of the ACCLS system anticipated to meet the needs of the FF are as follows: A portable, self-contained, lightweight (less than 80 lb), protected environment for one casualty, capable of providing sustained, critical care monitoring and automated life support for combat casualties for up to 24 hours on the FF Force (FF) Battlefield. System capabilities will include: 1) Integral suction and ventilatory capabilities 2) Automated external defibrillation system 3) Integrated parenteral infusion system 4) On-demand oxygen production capability with compatibility with external oxygen delivery systems 5) Physiological monitoring (non-invasive & invasive) including blood chemistries and BP, ECG, HR, Core temp, oxygen saturation 6) Protection from environment, biological & chemical agents 7) Data logging and transmission capacity 8) Compatibility with military vehicle and European power sources and 9) Automated life support functionality directed at conserving resources and manpower. External dimensions will be constrained to be no greater than the cube of the existing NATO litter to maintain compatibility with existing patient movement vehicles (air and ground) and other litter support devices (litter stands, wheeled gurneys, etc). The total weight of the system with a 220 lb patient will not exceed that which is manageable with a 4 person, 5th percentile litter team (about 300 lbs). Stand-alone battery operation with all life support functions operational shall be required for a minimum of 2 hours to accommodate the transfer time between the MTF and ambulance. The system must also comply with the environmental requirements of MIL STD 810E and 462D and must comply with all airworthiness requirements of the Army rotor wing and Air Force fixed wing environments.

1.2.2 Software

The software development process follows Cleanroom Software Engineering process. Cleanroom Software Engineering is a rigorous formal methods process for generation of software requiring high reliability and is a process that fulfills the requirements of the FDA for medical device development and code traceability. This process places a heavy emphasis on the prospective generation of requirements for software before any coding begins. Once the requirements are thought to be complete, the stimulus response table is constructed linking specific conditions or stimuli to the desired response. An enumeration process follows this, which is a mathematical procedure for determining canonical and illegal states. This eliminates redundancies and identifies impossible software states. From the results of the enumeration process, state boxes are generated, then clear boxes and finally the code is written. A testing protocol is then constructed based upon a usage model and bench level testing performed. This is followed by laboratory evaluation of controller performance in animal models of the pathophysiologic states expected in the course of evacuating the patient from the front to the rear.

2.0 CLOSED LOOP DEVELOPMENT APPROACH

The basic components of a closed loop control system include 1) a sensor for the parameter to be controlled, 2) a set point target for the controlled parameter, 3) a comparator, which generates an error signal based on the difference between the set point target and the present value, 4) a transfer function, which converts the error signal into a command instruction for the effector device and 5) the effector device which implements the appropriate corrective action. This control loop emulates the components and their relationships within the physiological control systems found in the human body, which are largely negative feedback loops.

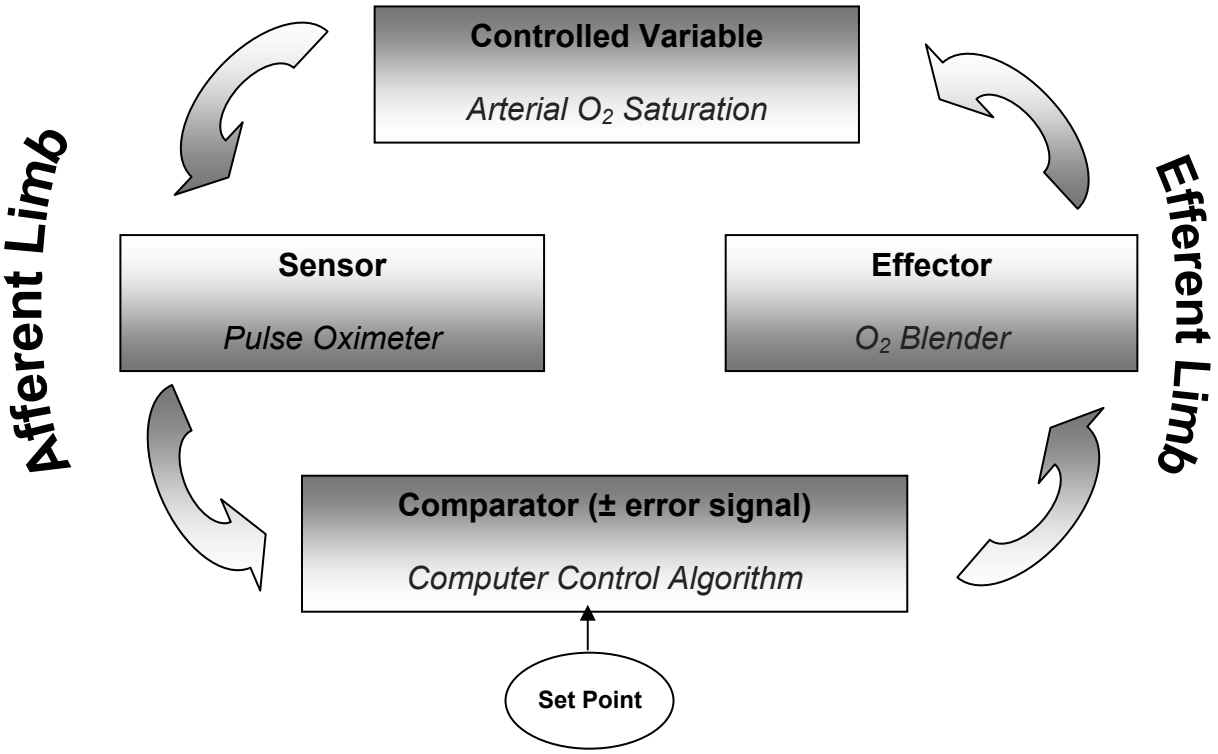

Fig. 1 Block diagram of closed loop control elements

Figure 1 shows the relationship of these basic closed loop components and illustrates the principle of automating the delivery rate of oxygen to the patient by driving the oxygen flow rate with the deviation of the measured arterial oxygen saturation from the desired set point.

2.1 Control of Intravenous Fluid Administration

Delivery of intravenous fluid for resuscitation in the field has been gravity-driven for more than 70 years. However, gravity-driven flow has several significant drawbacks in the field, including; 1) increased risk of exposure to enemy fire under battle conditions due to the need to hold the IV bag in the air, 2) a requirement for a fifth man to carry the IV bag in a 4-man litter carry 3) poor control of infusion rate and resuscitation. In addition, during air evacuation, previous commercial intravenous pump designs are difficult to keep running due to the small air bubbles that are produced as a result of off-gassing at altitude. These small bubbles cause the bubble detection feature to error and shut down the pump flow. Improved control of the rate and volume

of resuscitation fluid administered is required to allow implementation of new resuscitation strategies aimed at optimising tissue perfusion while minimizing fluid resource utilization. These problems could be overcome with an active pumping mechanism. Recognition of these field issues, led us to design and patent a new pumping mechanism, which will eliminate the aforementioned problems. This work uses the new commercial implementation of this patent that has the added feature of an analog control interface.

2.1.1 Control Software [Computer Assisted Resuscitation Algorithm (CARA)]

2.1.1.1 Set Point

The general strategy in the initial development of closed loop fluid resuscitation is not to discover a new resuscitation end point goal, but to simply emulate what is currently being practiced in the pre-hospital and emergency room settings today by infusing fluid to a target blood pressure end point. The classical clinical definition of shock includes systolic pressure of less than 90 mm Hg with tachycardia. Therefore, the CARA algorithm has been constructed with a blood pressure end point that would not qualify as shock by this definition. The CARA uses the mean arterial blood pressure setting as a target instead of systolic pressure since the mean pressure is less susceptible to problems encountered with improperly damped arterial pressure lines, which therefore mitigates a risk identified in the software hazard analysis. Although the mean arterial blood pressure default target is 70 mm Hg in CARA, this can be over-ridden by the care provider. The rationale for choosing this endpoint is based on the fact that autoregulation of blood flow is manifest, in most all organ systems, above a mean arterial blood pressure of 60 mm Hg. Furthermore, within the concept of operation for the use of the Automated Critical Care Life Support System, this device would serve as an asset of the Forward Surgical Team, where only resuscitative surgery would be done. In this context control of the bleeding may be tenuous and the risk of reinitiating bleeding with overly aggressive fluid resuscitation is significant. Thus, limiting fluid resuscitation efforts to sub normal blood pressure targets to minimize re-bleeding problems while providing adequate organ perfusion is the physiological goal around which CARA was designed. There is currently no other practical way to implement this strategy without automated control of fluid infusion rates since battlefield caregivers are not able to monitor the patient and titrate fluid continuously.

2.1.1.2 Comparator and Error Signal

The controller to be used is a Proportional, Integral, Derivative (PID) controller, which by definition has three components included in generation of the error signal; the proportional component, which is based on the absolute difference between the target and the current value, an integral component, which reflects the cumulative difference from the target pressure and a derivative component, which relates to the rate of change [25]. Currently it is not known whether all three of these components are required for effective control of the mean arterial blood pressure. Therefore, the coefficients on each component will be tracked throughout the resuscitation efforts to evaluate their relative contributions to the error signal. If a component contributes insignificantly regardless of the physiologic state of the animals for the type of resuscitation fluid, this component will be dropped in order to simplify the algorithm.

Clearly, the update frequency of the mean arterial blood pressure signal will significantly impact the effectiveness of the controller. Initial experiments have shown excellent control of blood pressure with five second updates of the mean arterial blood pressure, however, there are few non-invasive blood pressure sensors that can provide an update this frequently. Therefore, a major goal of this work will be to quantity the effect of blood pressure sampling frequency on the performance of the PID controller. PID controller performance will be evaluated by measuring 1) the time to achieve 50 percent and 90 percent of the target

blood pressure levels and 2) the 20 minute cumulative deviation (mmHg-min) from the target blood pressure once 90 percent of the target has been reached. In order to explore the effect of blood pressure sampling frequency on the blood pressure control, the sampling frequency of the arterial pressure line will be altered in 20 second increments starting at 5 seconds up to two minutes. These metrics of PID performance will also be quantified with each method of blood pressure measurement. The results of this series of experiments will quantify the effect on controller performance with different sampling frequencies for the blood pressure measurement. This data will be important in this selection of the blood pressure measurement modality as these data will allow for the potential of dynamically changing the sampling frequency to accommodate the clinical situation. For example, during circumstances where the desire for aggressive resuscitation is desired or circumstances where the blood pressure is falling in spite of the efforts of the controller, the sampling frequency can be increased to the level required to re-establish good blood pressure control. It is possible that oscillometric blood pressure cuffs may be sufficient in certain circumstances where the pressure is relatively stable, however a more rapidly responding sensor will be required to accommodate unstable conditions.

An adaptive quality may be conferred upon this algorithm if the responsiveness of the cardiovascular system to volume infusion is tracked as well. Therefore the pressure change associated with the volume infused will be tracked by the algorithm and will be expected to change with the state of the compensatory capability of the animal through the dynamic process of shock. It is expected that in the decompensatory phase of shock, it will be necessary to infuse more volume to attain the same pressure goal as the responsiveness of the peripheral vasomotor system deteriorates. We have observed that this low peripheral resistance state also occurs in normovolemic animals with 2.5 percent isofluorane anaesthesia in this model and therefore could serve as a surrogate for the decompensatory phase of hemorrhagic shock which is also characterized by a lack of vasomotor responsiveness to fluid and to catecholamine therapy. It is a goal of these experiments to record the pressure-volume history accumulated during operation of the controller during resuscitation to determine whether it will be possible to confer an adaptive change in the PID controller that would accommodate these pathophysiologic changes in the cardiovascular system. This information might also trigger an informational alert to the user to indicate that there is been a change in the physiologic state of the vascular system that might cue either the onset of vascular decompensation, correlate with a pharmacological effect of a drug infusion (e.g. isofluorane-induced vasodilatation), or indicate volume loss from the system, such as onset of bleeding. The protocol described below addresses this issue by proposing to undermine the controller's efforts by removing blood at controlled rates to determine whether it might be feasible to detect the onset of occult bleeding.

2.1.1.3 Transfer Function

The transfer function will convert the error signal from the PID in mm Hg to a driving voltage for the pump that translates to a flow rate in ml per minute.

2.1.2 Sensor and Effector Hardware

2.1.2.1 Infusion Pump

Since there were no commercially available fluid infusion pumps which could deliver flow rates high enough for resuscitation of hemorrhagic shock, we (WRAIR) designed and patented a new, light weight, and highly efficient pumping mechanism which would meet the needs for fluid resuscitation in echelon I. The pump dimensions are 2.4"W x 3.8"L x 1.2"H and weighs 238 grams. This pump is FDA approved and is in production (Infusion Dynamics, Inc., Plymouth Meeting, PA) and is composed of three basic parts 1) a reusable control unit, 2) a sterile disposable cartridge and 3) a single-use battery, lasting 6 hrs at 100 ml/min.

It uses a sterile disposable pumping cartridge with standard Luer fittings and a built-in air eliminator. The air eliminator prevents the pump from shutting down due to off gassing at reduced atmospheric pressures, such as that encountered during air evacuation. The pump can operate as a stand-alone device with the flow rate set using a knob on the side of the pump or it can be controlled by a signal from an external device. This latter feature allows implementation of servo-controlled fluid resuscitation based on blood pressure or any other selected resuscitation end-point. The lightweight nature of the pump allows it to be attached to the patient's arm with a Velcro strap.

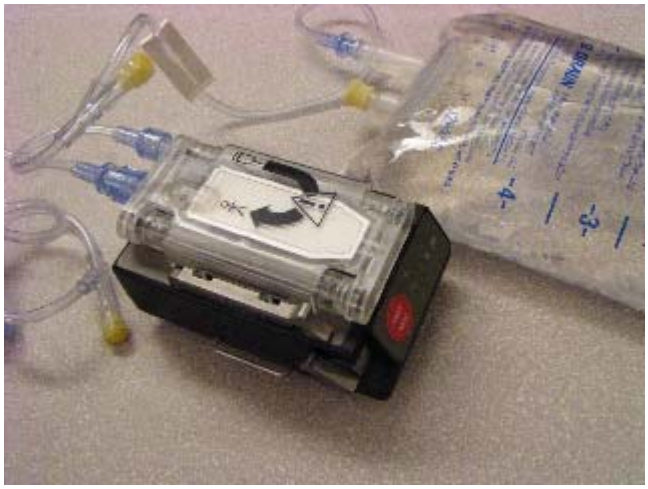

Fig. 2: Picture of intravenous infusion pump with 500 ml bag of Hespan

The one-way valve arrangement and non-occlusive pumping action allows fluid to flow freely in the forward direction only. The IV lines can be primed or purged of air by simply squeezing the IV bag. This free flow feature also provides for fail-safe operation since fluids can be delivered by elevating or pressurizing the IV bag while the pump is off but still connected. The pump infuses crystalloids at rates comparable to an IV bag raised 7 feet above the patient and colloids at rates comparable to a bag raised 15 feet (6 L/hr.). Compared to inflatable pressure infusers, this pump offers typically shorter set-up times, an air elimination filter and greater control over flow rates. This latter feature is important to enabling the hypotensive resuscitation strategy to be implemented in the field as a temporizing resuscitation strategy which will minimize the potential for re-bleeding during resuscitation efforts aimed at elevating the arterial blood pressure. The electrical impedance of the infusion fluid past the air eliminator is continuously monitored and will shut down if a bubble is detected or a fluid below physiologic ionic strength is pumped. The latter prevents accidental infusion of distilled water or other fluids of unacceptable ionic strength. Alarms are also triggered with conditions of low battery and IV tube occlusion. A new cartridge allows for infusion of whole blood as well.

In the experimental animal studies, the flow delivered to the animal is quantified by the decrease in the weight of the infusion bags resting on a digital scale. Obviously, in the final of implementation of CARA, there must be a way to relatively accurately quantify the volume infused in order for the tracking of the pressure-volume history to be useful in conferring an adaptive component to the controller or to be able to issue an advisory on the change in the physiologic response to the volume as suggested above. Currently there is no flow monitor built into the infusion pump but clearly this would be a hardware improvement that would be desirable for the

reasons cited above. However, the back emf is measured which gives an indication of the motor speed that is used to validate that the motor performance is appropriate for the driving voltage instruction issued by the controller. This gives only a semi-quantitative estimation of the actual flow since other factors such as the inlet and outlet pressures can affect the absolute flow rate. Studies are ongoing to determine whether the back EMF might be accurate enough for predicting the flow with varying inlet and outlet pressures. If not, a recommendation to add a flow monitor to the pump will be made to the manufacturer for this application.

2.1.2.2 Blood Pressure Sensor

Obviously a major component of importance is the sensor responsible for measuring the mean arterial blood pressure. The sensor must be reliable, be able to provide continuous blood pressure measurements and preferably be non-invasive. The greatest reliability and accuracy is obtained from an arterial line but its invasive nature makes it undesirable for the patient on the move in the battlefield setting. However, the most ubiquitous non-invasive alternative, which is the oscillometric blood pressure cuff, cannot be used for long periods of time at sampling frequencies > twice per minute and is susceptible to motion artefact and error in high vibration environments.

Clearly, the quality of the blood pressure measurements will significantly affect the performance of the controller, however, it is not clear what the lowest blood pressure measurement frequency can be an still get good blood pressure control. Therefore, the current studies will systematically study the effect of blood pressure measurement frequency on blood pressure control using an intra-arterial blood pressure line sampled at different frequencies. This information is required for selection of the best non-invasive blood pressure measurement modality. Currently, there are three non-invasive monitoring techniques that will be evaluated against the arterial line standard for their ability to provide pressure readings of sufficient quality and frequency to meet the requirements of optimal blood pressure control. A standard oscillometric blood pressure cuff will also be included for a basis of comparison. If new options become available, they will also be evaluated.

2.1.3 Controller Performance

Figure 3 illustrates the type of experiment that is used to evaluate the performance of the closed loop controller, CARA. In this experiment, the experimental protocol was designed to emulate a severe arterial bleed in 70 kg swine resulting in a drop in the mean arterial blood pressure (MABP) to 40 mm Hg over a 15 min period. The pressure was then held there for 15 min. This resulted in the loss of 1.45 L of blood or 30% of the pig's blood volume. Resuscitation was then initiated by turning on the autocontrol software which ran on an external computer which was receiving mean arterial blood pressure readings every 5 s, calculating the deviation from the target and then applying the transfer function to alter the driving voltage every 5 sec. The volume infused was followed by monitoring the output of a digital scale on which the resuscitation fluid was placed. In this experiment, the MABP set point was 70 mm Hg and the resuscitation fluid was 0.9% saline. Metrics of the controller performance are shown in the table above the graph showing the times and volumes required to attain 25, 50, 90 and 100% of the MABP target. Although 90% of the target value was attained with 756 ml of saline within 6.3 min with the pump operating continuously at 120 ml/min, an additional 1.5 L was required to maintain the MABP at this level for the next 30 min. Comparison of the dotted line drawn over the resuscitation period shows excellent control of the blood pressure over the 40 min following the start of resuscitation. This figure also shows the effect of a transient occlusion of the pump outflow tract at 48 min that initiated the occlusion alarm. When the occlusion was released, the autocontrol resumed automatically and restored the blood pressure once again as it had fallen as a result of the 2 min occlusion.

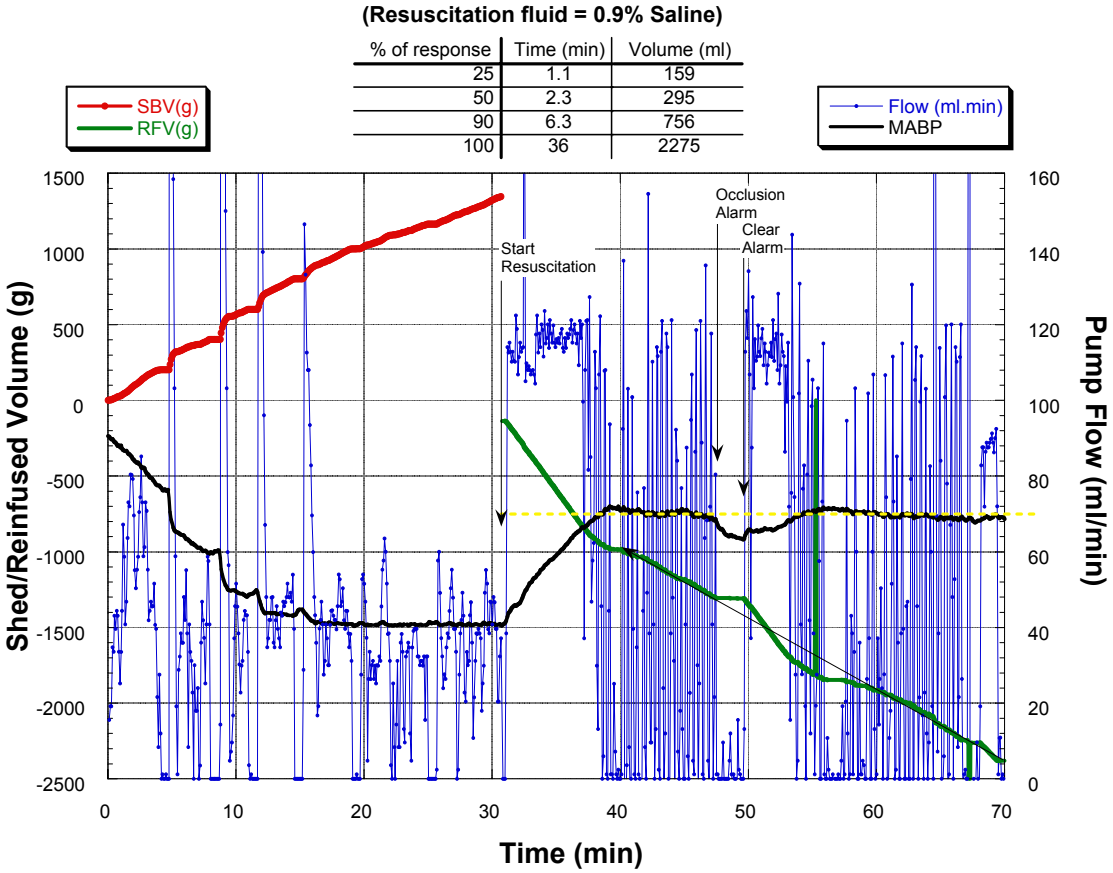

Fig. 3 Example of PID Closed Loop Control of Arterial Blood Pressure during Resuscitation

2.2 Control of Ventilation

Seventeen per cent (17%) of patients seen by the Marine Forward Resuscitative Surgery Units during the first 30 days of Operation Iraqi Freedom required en route care and 20% were categorized as unstable. The mean time to evacuation was 8 hours and patients who were intubated and/or required ventilation accounted for 25% of the 48 indications for en route care. Since Army Medevac is staffed by only by flight medics who are not trained in ventilator management, it is important to automate ventilator operation so that minimal training, or even no training, is required for them to safely transport the critically injured patient. Currently, neither the Marine Corps FRSS or the Army FST have enough medical personnel who are familiar with ventilator operation that they can afford to lose them on a Medevac mission.

The modern mechanical ventilator has been in existence for nearly 100 years. The earliest efforts focused on ventilating the patient by applying a negative pressure in a closed space in which the patient was contained from the neck down. This iron lung concept evolved in the mid 20th-century to ventilation using intermittent positive pressure via an integrated airway. It was not long after the first automatic mechanical ventilator was developed that investigators began exploring ways to automatically control ventilator in response to patient needs. Frumin developed the first working closed loop controller based on the automatic maintenance of end-tidal CO_2 levels [5]. This system simply changed the tidal volume in small steps until the desired change in

CO_2 level was achieved; requiring an increase in the tidal volume to decrease the end tidal CO_2 levels. [12], implemented a closed loop control system based on arterial PO_2, and demonstrated maintenance of the arterial oxygen tension within 1 mm Hg of the target value even when CO_2 production rates were increased by nearly 50 percent. Chapman [2] described similar precise control of end-tidal CO_2 levels, achieving the set point goals within 60 seconds of the set point change and maintaining the end-tidal CO_2 level to within 1 percent of the set point. However, controllers that use end-tidal CO_2 levels presume that this measurement is a reasonable estimate of arterial PCO_2. This is the case as long as there are not ventilation-perfusion mismatches that create large alveolar to arterial gradients such as those observed during embolic events or in atelectasis. In these cases, the end-tidal CO_2 partial pressure decreases and the controller's response is to decrease the ventilation in an attempt to increase the end tidal CO_2 levels. This is an inappropriate response. Therefore, unless ventilation perfusion mismatches can be ruled out end-tidal CO_2 controllers are not safe.

In addition, successful control of ventilation has been achieved using intra-arterial blood pH monitors as well [4]. The principal of this control system is to adjust the arterial PCO_2 to maintain a pH of 7.4 according to the Henderson-Hasselbach equation; $pH=6.1 + \log[HCO3]/(.0301 * PCO_2)$. This controller would be expected to work well under conditions of metabolic acidosis and controlled ventilation, where the respiratory muscles are paralyzed and unable to respond to the chemoreceptor-mediated drive. The commercial availability of intra-arterial PCO_2 and pH monitors make controllers that use these endpoints feasible today.

Closed-loop ventilation has been a topic of active investigation for over 50 years and ventilator companies in Europe and the US have positioned their hardware for closed loop control for some time. However, at present, closed-loop ventilator systems have only been licensed for sale in Europe.

2.2.1 Software Controller

The overall approach to maintaining arterial oxygen saturation will be to first optimize oxygenation by means of ventilator adjustments (i.e. tidal volume, frequency, I:E ratio, PEEP) and then to only deliver oxygen when increases in alveolar ventilation do not resolve the desaturation problem. Evaluation of the performance of the ventilator and oxygen flow controller will first be tested independently and then in combination during specific ventilatory challenges designed to emulate anticipated clinical conditions. Once these controllers are operating satisfactorily in an independent manner, they will be evaluated together. The final phase will evaluate the combined CARA and CAVA algorithms operating simultaneously.

2.2.1.1 Set Point

In view of the problems noted above with regard to controllers that are based on end-tidal CO_2 , and their inappropriate response to ventilation and perfusion mismatch conditions, a review of the literature shows that a relatively new controller developed by Laubscher offers significant advantages [7,8]. The closed loop controller that will be evaluated for inclusion into the ACCLS system in this proposal is called Adaptive Volume Ventilation which uses breath to breath analysis of the pressure volume relationship to determine the optimal tidal volume and respiratory rate required to minimize the work of breathing while achieving a minute ventilation goal which is set by the user. The advantage of this type of controller is that it is based on a physiological principal discovered by [14] who demonstrated that mammals normally breathe at tidal volume and respiratory rates that minimize their work of breathing. This is been shown to work particularly well for weaning ventilator-dependent patients in a shorter amount of time [10]. This technique is also suitable for use in both spontaneously breathing as well as paralyzed patients. The only input required from the user is an approximation of the desired gross alveolar ventilation set point, which is simply the product of the respiratory rate and tidal volume minus the anatomical dead space volume. To avoid having to set this value,

the test breath procedure described by Laubscher et al. will be used [7]. This test procedure uses a standardized breath pattern based on pressure controlled synchronized intermittent mandatory ventilation (PCSIMV) and requires synchronized measurement of airway flow, airway pressure and instantaneous expired CO_2 concentration. These breaths are analyzed in terms of tidal volume, series dead space and respiratory time constant. With knowledge of the respiratory rate the gross alveolar ventilation can be calculated based on these test breaths to initiate the ventilation start up procedure. Comparator and Error Signal

The work of breathing (WOB) calculation will be performed twice per minute and compared with the prior WOB and changes tracked.

2.2.1.2 Transfer Function

The tidal volume and frequency required to minimize the work of breathing in accordance with the work of Otis [14], will be calculated for the target gross alveolar ventilation set point as described by Laubscher [7] and the optimized settings sent to the ventilator twice per min.

2.2.2 Sensor And Effector Hardware

2.2.2.1 Sensors

Calculation of the WOB required a measurement of lung compliance which is derived from instantaneous measurement of the airway pressure and flow. Assessment of SPO_2 and end tidal CO_2 is required periodically to assure that gas exchange is adequate at the chosen gross alveolar minute ventilation. To determine whether this level of alveolar ventilation is sufficient requires periodic blood gas analysis. Within the context of the ACCLS system, it is proposed that this data be input by the user who may periodically analyze blood samples using a handheld point of care blood analysis system or the commercial intra-arterial PCO_2, pH and PO_2 fiber-optic probes may be used for continuous update of the arterial PCO_2 values. If this number is available, the gross alveolar ventilation can be automatically adjusted to compensate for any ventilation perfusion mismatch conditions that create a large alveolar to arterial gradient. This can only be done however, if the arterial CO_2 tension is known so that the gross alveolar ventilation can be corrected for the alveolar dead space ventilation. With this level of automated control the ventilator control panel could be reduced to a single knob for setting the alveolar ventilation in liters per minute, which can be simply done on the basis of a lookup table that shows minute ventilation as a function of body weight.

2.2.2.2 Ventilator

This effort will seek to adapt the preferred patient movement item (PMI) transport ventilator chosen by the Armed Services to be used in the context of en route care. Recently Impact Instrumentation, Inc. has modified its 754 series ventilator for digital control, enabling it to be microprocessor-controlled. The first phase of this effort will be to evaluate the effectiveness of the adaptive volume ventilation controller when implemented on this ventilator. These studies will be conducted in both spontaneously breathing and paralyzed and anesthetized 70 kg swine.

2.3 Control of Oxygen Administration

The US Army Combat Support Hospital planning factors for oxygen, call for 9 tons of oxygen per day (including the weight of the cylinders) to support the oxygen needs of a 256-bed hospital. This massive

requirement is logistically difficult to manage and oxygen tanks are a significant safety hazard. As a result, the Army Medical Department has initiated an effort to eliminate oxygen tanks from the battlefield and to replace them with oxygen generation systems. Both the US Army and the Air Force have significant investments in this area. However, the systems under development have been oriented toward meeting the needs based on utilization within civilian fixed facility hospitals where oxygen is considered inexpensive and readily available. As a result, efforts to conserve oxygen in the civilian medical setting have not been considered important.

Oxygen conservation systems are in common use within the diving community but have not found their way into the medical community, probably because oxygen conservation has not been a primary concern. Although the closed loop system with CO_2 absorbant is the best suited to achieving the greatest degree of oxygen conservation, its complexity is one negative aspect. Other alternatives that can accomplish conservation of intermediate value are also possible. Although not optimal, there are passive partial re-breathing approaches that have recently been commercialized that would allow a 50% decrease in flow rate to achieve the desired FIO_2 (i.e. Hyox partial re-breathing mask). In addition, pulse conservation methods are also available which deliver oxygen only during inspiration. This technique saves two-thirds of what would normally be delivered in a continuous flow, non-re-breathing circuit with an I:E ratio of 1:2. This feature is commonly found in home care oxygen delivery systems that use nasal cannulas. Each of these techniques, combined with continuous monitoring of the arterial oxygen saturation from pulse oximeter readings will allow the system to consume as little oxygen as possible while meeting the oxygenation requirements of the patient.

Closed-loop controllers have been reported recently to be very effective in maintaining the arterial oxygen saturation within 3% of the target SpO_2 in mechanically ventilated patients [19] and to be as effective or more effective than a full time nurse in maintaining the SpO_2 of low birth weight infants within a normoxic range of 88-96% [3]. Similar studies have not yet been done in trauma patients.

2.3.1 Software Controller for Oxygen Administration

Advanced Trauma Life Support (ATLS) guidelines recommend 10 to 15 L/min supplemental oxygen flow for all trauma patients. Furthermore, the ACCLS platform will need to carry intrinsic oxygen delivery capability in order to accommodate patients with either pulmonary compromise or respiratory control problems caused by head injury and to accommodate treatment at altitude. However, in the context of the ACCLS development effort, it is an objective consistent with the goals of the Combat Developer, to provide oxygen with on-demand oxygen generation systems in order to eliminate the use of oxygen cylinders on the battlefield. However, with the current state of oxygen generation systems, units that generate 10 to 15 L/min weigh nearly 100 lbs. To meet the weight goals of the ACCLS platform, it will be necessary to minimize the size of the oxygen generation system required to maintain the arterial hemoglobin oxygen saturation goals. Current MRMC investments have produced a pressure swing oxygen generation system that will deliver 3 L/min and weighs between 8 and 10 lbs. Although this is a significant improvement over pervious systems, this weight is till too much as it represents a 10 to 15% of the total weight of the system. Clearly, it will require a significant oxygen conservation effort to enable the size of the generation system to be reduced even further. Consideration of the factors leading to the high recommended oxygen flow rates suggest that the recommendations for these flow rates pre-dated the wide-spread availability of pulse oximeters and were aimed at covering 100% of the minute ventilation requirements of adults of any size. In addition, these high rates also help to overcome the air admixture problem that non-re-breathing oxygen masks have.

2.3.1.1 Set Point

In the context of the ACCLS development, it is useful to consider how low the oxygen flow rate can be and still meet the patient requirements throughout the whole range of clinical conditions encountered in the battlefield and during air evacuation where $FI0_2$ is reduced in proportion to the altitude/atmospheric pressure. The theoretical limit for oxygen flow that which is equal to the oxygen consumption of the patient. At rest, the oxygen consumption of a typical 70 kg man is 200 to 250 ml/min. With sedation or anesthesia, this value is decreased by 25 to 30%. This rate is at least 50 fold lower than the recommended ATLS flow rates. If the oxygen generation systems were linearly scaleable, the theoretical weight of an oxygen generation system capable of 0.3 L/min would be 1 to 2 lbs. To accomplish this theoretical limit would require a sealed re-breathing circuit with CO_2 absorbent and oxygen titrated into the circuit to maintain a constant $FI0_2$. Any $FI0_2$ could be achieved by briefly flushing the inspiratory side of the breathing circuit with higher flow rates. This would be necessary in patients with large alveolar to arterial (A-a) gradients due to ventilation-perfusion mismatch or edema. Once the desired $FI0_2$ is attained, the steady state flow required to replace the consumed oxygen will be re-established and will be equal to the rate of oxygen consumption in a closed system. Thus, recording the flow rate required to replace the oxygen consumed would provide a continuous monitor of patient oxygen consumption, which is an excellent end point for resuscitation. The set point for oxygen saturation will be 90% as assessed by arterial blood gas measurement or pulse oximetry.

2.3.1.2 Comparator and Error Signal

The deviation from the arterial oxygen saturation set point will be calculated every 30 sec and the oxygen flow will be altered to accomplish the flow change using a PID controller constructed in an analogous manner to the fluid infusion algorithm described above. In both cases, the active control is unidirectional, that is, the administration rate of oxygen can be increased or decreased but cannot be removed from the system to compensate for overshooting the target. The controller can only turn off the flow and then allow passive return of the controlled variable toward the set point. Physiological factors outside of the controller's influence will determine this rate of return toward the target in these "overshoot" situations.

2.3.1.3 Transfer Function

The error signal will be converted to an instruction to the oxygen blender contained within the ventilator, to digitally alter the FIO_2 setting in accordance with the PID derived error signal.

3.0 CONCLUSIONS

Automation of the life support systems is a critical capability that will allow expedient movement of casualties out of the FST and will level the quality of care throughout the echelons of medical care of the critically injured. The ACCLS capability proposed here would provide automation of life support functions, providing computer-driven closed loop control of ventilation, fluid, drug and oxygen administration in the first iteration. This system would optimize the patient's treatment, while minimizing resource utilization (i.e. oxygen and resuscitation fluid). The ACCLS platform will also be a significant critical care enabler for the small FST staff and for the 91W staffing the air and ground ambulances. The closed loop Automated Critical Care Life Support System will provide improved holding capability at the FST as well as extended critical care capability within ground and air ambulance platforms by providing automated life support for the critically injured during the evacuation and holding process.

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